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[E-mail Article](#)**Pharmacodynamics of insulin in polyethylene glycol-coated liposomes**Anna Kim<sup>a</sup>, Mi-Ok Yun<sup>a</sup>, Yu-Kyoung Oh<sup>a</sup>, Woong-Shick Ahn<sup>b</sup> and Chong-Kook Kim<sup>a</sup><sup>a</sup> College of Pharmacy, Seoul National University, Shinlim-dong, Kwanak-ku, Seoul 151-742, South Korea<sup>b</sup> College of Medicine, The Catholic University of Korea, Banpo-dong, Seocho-gu, Seoul 137-140, South Korea

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**Abstract**

To reduce the injection frequency and toxicity of intravenously administered protein drugs, it is necessary to develop safe and sustained injectable delivery systems. In this study, to evaluate liposomes as safe and sustained injectable delivery systems of proteins, we chose insulin as a model protein drug and tested its incorporation efficiency and pharmacodynamics in various liposomes with and without polyethylene glycol (PEG)-derivatized phospholipid. The liposomes coated with PEG showed 3-fold higher efficiency of insulin incorporation than did the liposomes without PEG. Moreover, among the liposomes coated with PEG, dipalmitoylphosphocholine (DPPC) liposomes showed higher incorporation efficiency than did dimyristoylphosphocholine (DMPC) liposomes. For pharmacodynamic study, insulin (2 IU/kg) was administered in various formulations, such as insulin alone in phosphate-buffered saline and insulin in the DPPC liposomes with and without PEG, to streptozotocin-treated diabetic rats. The pharmacodynamics of insulin alone, however, could not be measured due to the immediate death of rats caused by hypoglycemic shock. In contrast, all the rats treated with liposomal insulin survived, probably by the sustained release of insulin from liposomes. Pharmacodynamics of liposomal insulin showed that PEG-coated liposomes induced the lowest level of blood glucose—the nadir—1 h later than did the liposomes without PEG. These results indicate that PEG-coated liposomes could be

developed as a relatively safe and sustained injectable delivery system for insulin with improved incorporation efficiency. Moreover, it is suggested that the liposomes coated with PEG might have a potential as safe injectable delivery systems for other protein and peptide drugs.

**Author Keywords:** Incorporation; Insulin; Liposomes; Pharmacodynamics; Polyethylene glycol

**Index Terms:** liposome; insulin

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**PURPOSE:** The mucoadhesiveness of polymer-coated liposomes was evaluated to develop a novel drug carrier system for oral administration of poorly absorbed drugs such as peptide drugs. **METHODS:** Multilamellar liposomes consisting of dipalmitoylphosphatidylcholine (DPPC) and dicetyl phosphate (DCP) (DPPC: DCP = 8:2 in molar ratio) were coated with chitosan (CS), polyvinyl alcohol having a long alkyl chain (PVA-R) and poly (acrylic acid) bearing a cholesteryl group. The adhesiveness of the resultant polymer-coated liposomes to the rat intestine was measured in vitro by a particle counting method with a Coulter counter. The CS-coated liposomes containing insulin were administered to normal rats and the blood glucose level was monitored. **RESULTS:** The existence of polymer layers on the surface of liposomes was confirmed by measuring the zeta potential of liposomes. The CS-coated liposomes showed the highest mucoadhesiveness and the degree of adhesion was dependent on the amount of CS on the surface of the liposomes. The blood glucose level of rats was found to be significantly decreased after administration of the CS-coated liposomes containing insulin. The lowered glucose level was maintained for more than 12h after administration of the liposomal insulin, which suggested mucoadhesion of the CS-coated liposomes in the intestinal tract of the rats.

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